

REMARKS

Claims 1-29 are pending in the application. For convenience, the Examiner's rejections are addressed in the order in which they were presented in the April 9, 2003 Office Action.

*Objection to the claims*

Claims 25-27 were objected to as reciting abbreviations without providing proper explanations of the abbreviations. Claims 25 and 26 have been amended to recite "G-protein coupled receptor B3" and "G-protein coupled receptor B4." Claim 27 has been amended to correct the typo "HEK-93" and to recite "HEK-293," which is the name of a cell line well known to those of skill in the art, as described in the specification on page 33, line 2.

*Rejection under 35 U.S.C. § 103*

The claims were previously rejected as allegedly obvious over Margolskee in view of Ray or Levine. In the April 9, 2003 Office Action, the Examiner further rejected the claims as obvious over Margolskee in view of Burtch and further in view of Negulescu, as well as in view of Ray and Levine.

As previously discussed, Margolskee discloses Gustducin, a G-protein alpha subunit specifically expressed in taste cells. Margolskee also teaches generally that compounds that modulate taste may be identified using assays for taste cell specific proteins involved in taste transduction, such as Gustducin. Margolskee does not disclose the taste cell specific G-protein beta subunits of the present invention.

Ray and Levine disclose G-protein beta subunits with identity to the claimed polypeptides. The polypeptide of Ray was cloned from a heart cDNA library, and expression of the mRNA encoding the G-protein beta subunit was shown in heart and brain. The polypeptide of Levine was cloned from a retina cDNA library, and expression was shown in four different cell lines: rhabdomyosarcoma, pheochromocytoma, neuroblastoma, and dermal

fibroblasts. Neither Ray nor Levine disclose that the G-protein beta subunit is expressed in taste cells of the tongue.

As described by the Examiner, the newly cited Burtch reference teaches the "involvement of the common G protein beta subunit in the taste plasmi membranes." The Examiner further states "[w]hile the reference does not teach the amion acid sequence of the  $\beta$  subunit, Examiner takes the position that such amino acid sequences are inherent to the polypeptide and therefore the reference  $\beta$  subunit has an amino acid sequence that is identical to that of either SEQ ID NO:3 or 5 or that its amino acid sequence is greater that 70% identical to that of SEQ ID NO:3 or 5." Office Action, page 5, lines 15-19.

As described by the Examiner, the newly cited Negulescu references teaches the use of promiscuous G-proteins.

Applicants respectfully traverse the rejection. The present invention demonstrates for the first time a G-protein beta subunit preferentially expressed in taste cells of the tongue. As such polypeptides were not previously known to be expressed in the tongue and involved in taste signal transduction, one of skill in the art would not have been motivated to use the proteins of Burtch, Ray, or Levine in the taste transduction assay methods of Margolskee.

In the rejection, the Examiner concludes that the presently claimed invention would be obvious, without identifying the principles that would motivate one of skill in the art to combine the cited references. By using hindsight to provide the requisite motivation, the Examiner has failed to make a prima facie case of obviousness. *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998). As discussed by the Federal Circuit in *In re Rouffet*,

Because the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness" (*In re Rouffet*, 47 USPQ2d at 1458).

Ray teaches a G-protein beta subunit that has 100% identity to SEQ ID NO:3 of the present invention. Levine teaches a G-protein beta subunit that has 97% identity to SEQ ID NO:5 of the present invention. However, the protein of Ray was cloned from a heart cDNA

library, while the protein of Levine was cloned from a retina cDNA library. Expression of these polypeptides were shown in the heart and brain (Ray) and in in four different cell lines: rhabdomyosarcoma, pheochromocytoma, neuroblastoma, and dermal fibroblasts (Levine). Notably, these references fail to teach or suggest that these G-protein beta subunits are expressed in taste cells, or are in any way involved in taste signal transduction. Therefore, one of skill in the art would not be motivated to use the polypeptides of Ray and Levine in the taste transduction assays of Margolskee. Margolskee only provides general guidance regarding taste transduction assays, and fails to teach the polypeptides of the invention.

The Examiner attempts to provide the requisite motivation by citing Burtch as teaching that a G-protein beta subunit is expressed in taste cells. However, as acknowledged by the Examiner, Burtch fails to provide an amino acid sequence for the G-protein beta subunit. As Burtch fails to provide an amino acid sequence, one of skill in the art would not know if the Burtch G-protein beta subunit has the same or related sequence to the presently claimed G-protein beta subunit, or indeed the same or related sequence as the G-protein beta subunit described in Ray and Levine. Therefore, one of skill in the art would not be motivated to combine the teaching of Burtch with the teachings of Margolskee, Ray, or Levine to produce the current invention.

Furthermore, since Burtch fails to provide an amino acid sequence for the G-protein beta subunit, it is not an enabling reference because it fails to teach on of skill in the art how to make the G-protein beta subunit. Without a sequence, the chemical structure of a protein cannot be envisioned and synthesized. As described in MPEP § 2121.02, "[w]here a process for making the compound is not developed until after the date of the invention, the mere naming of a compound in a reference, without more, cannot constitute a description of the compound." *In re Hoeksema* 399 F.2d 269, 159 USPQ 596 (CCPA 1968).

Finally, the Examiner attempts to characterize undisclosed amino acid sequence as an "inherent property" of the protein. However, as described in the MPEP § 2112, "the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). In order to establish inherency, "the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described

in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 169 F.3d 743,745, 40 USPQ 323,326 (CCPA 1981). The Examiner appears to be using impermissible hindsight in order to attribute a sequence to the G-protein beta subunit of Burtch. No evidence has been provided demonstrating that those of skill in the art at the time of the invention would necessarily recognize that the protein of Burtch has the same or a similar amino acid sequence as the protein of Ray or Levine. Therefore, Burtch cannot be combined with Ray or Levine and Margolskee to demonstrate obviousness of the claimed invention.

The cited references, either alone or in combination, thus fail to teach or disclose the claimed invention. Applicants therefore respectfully request that the rejection be withdrawn.

#### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



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